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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KETTER, JAMES S	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 01/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,347	SEYMOUR ET AL.	
	Examiner	Art Unit	
	James S. Ketter	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-34 and 36-66* is/are rejected.

7)☒ Claim(s) *35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 June 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 35 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-34, 36-42, 44-64 and 66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is made for the reasons of record set forth in the Office Action mailed 10 March 2005.

In the paragraph bridging pages 10 and 11 of the amendment filed 28 October 2005, Applicants argue that one of skill could have selected hydrophilic groups to be transformed into reactive groups which would complement the surface of the biological element, based upon knowledge of the chemical nature of the groups present on said surface. However, given the complexity of cells and viruses, and the uncharacterized state of the vast majority of cell surface components, and the complexity of predicting the exact folding of proteins such that the precise nature of the exposed surface of each such protein would be evident, such knowledge did not appear to be available to one of skill such as to permit practice of the claimed invention. As

such, it would not have been apparent to one of skill in the art the Applicants were in possession of the full scope of the claimed invention at the time of filing.

Claims 58-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a new grounds of rejection.

The following factors have been considered in the rejection:

The nature of the invention. The invention of claim 58 encompasses a pharmaceutical for a gene therapy method, and as such, the recited method must be therapeutically useable for the composition to be enabled. Claims 59 and 60 are drawn to methods of gene therapy.

The amount of direction or guidance presented in the specification, and the presence or absence of working examples.

The specification as filed teaches no actual showing of successful treatment of a defect employing gene therapy techniques. No discussion of what levels of expression of any protein would be required to treat a disease using gene therapy is offered. Furthermore, no teachings with respect to a choice of vectors or amount of nucleic acid to be administered, for any particular disease condition, nor teachings with respect to the location of such administration are set forth. These factors would have to be determined by trial-and-error methodology.

The state of the prior art, and the predictability or unpredictability of the art. Generally, the prior art had seen no successes in treatment methods of either the in vivo or the ex vivo type of gene therapy. Several reviews of the art are discussed below, which show that the problems of vector selection and, more importantly, persistence of predictable and useable levels of expression of the therapeutic protein, represented technical barriers to the practice of gene therapy methods. Verma et al. (U, newly cited) teaches, e.g., at the four paragraphs at page 240, starting with the paragraph bridging the left-hand and center columns, and ending with the second full paragraph at the right-hand column, that persistence of expression and adequate expression systems, i.e., enhancer-promoter combinations, were problematic in gene therapy methods tried through that time. Furthermore, Table 2, at page 242, shows that none of the transfection systems extant at the time were suitable for actual treatment methods. Anderson (V, newly cited) sets forth the state of the art as of 1998. Specifically, Anderson makes clear that methods extant in the art, particularly vector selection, delivery methods and persistence of gene expression, were still inadequate to permit routine practice of the gene therapy, let alone any demonstrably successful practice at all. Both the first paragraph, left-hand column, at page 25 and the conclusory paragraphs at page 30 make clear that Anderson did not regard practice of gene therapy methods at all routine as of 1998. More recently, Juengst (W, newly cited) has taught that the actual outcome of a gene therapy method is much less predictable than previously hoped, due to pleiotropic effects, and that only a few apparent successes have been seen, with 2 of 9 of which patients later developing T-cell acute lymphoblastic leukemia as a result of the inserted genetic material altering expression of a particular gene, LMO-2. Thus, it is clear that as

of the filing date of the instant invention, gene therapy was regarded as essentially without successes and unpredictable

The quantity of experimentation. It is clear from the art, as shown by Verma et al., Anderson or Juengst, cited above, that a very large amount of experimentation had already been underway in the art as of 1997, 1998 and even 2003. Even with that amount of work, no successful gene therapy methods had been demonstrated. The references acknowledge the need for more work as of those dates. See, e.g., Verma et al. at page 239, at the first two introductory paragraphs; Anderson, e.g., at page 25, also at the first two introductory paragraphs, and the last two paragraphs at page 30; and Juengst at the first three paragraphs.

The breadth of the claims. The instant claims are drawn to the potential treatment of a wide variety of disease states, and to a potentially wide variety of methods or techniques used in such treatment. As such, the claims would have been regarded by one of skill as very broad.

Conclusion. Were the skilled practitioner to have attempted to make a pharmaceutical compound to practice the recited gene therapy methods, or to actually practice the claimed gene therapy methods, said practitioner first would have turned first to the specification for guidance in selecting dosages, treatment regimens and other factors which may bear upon the success of such treatment. However, as set forth above, such guidance in the specification is very limited in nature, and is insufficient with respect to prediction of proper levels of expression. Said practitioner then would have turned to the prior art to obtain detailed guidance for practice of the claimed methods. However, as set forth above, the prior art does not recognize any clearly successful gene therapy methods. Instead, the high degree of unpredictability of the art is taught, especially in the latest cited reference, Juengst. Thus, the skilled practitioner would not have

been able to find the necessary guidance in the prior art. Finally, said practitioner would have been forced to turn to empirical experimentation to determine appropriate dosages, treatment regimens and other factors, required for successful practice of a gene therapy method. However, as set forth above, the amount of experimentation recognized by the art as required for development of a successful gene therapy protocol is very large, and of a largely trial-and-error nature. Furthermore, as set forth above, the field of gene therapy is unpredictable. A large amount of experimentation in an unpredictable art with little or no available guidance is clearly undue experimentation.

Claims 58-60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record set forth in the scope-of-enablement rejection under 35 USC § 112, first paragraph, in the previous Office Action, mailed 10 March 2005. (Please note that this rejection employs the same logic and grounds of rejection as the scope-of-enablement rejection, below, also maintained from the previous Office Action. In essence, the scope-of-enablement rejection from the previous Office Action has been split into this enablement rejection and the following scope-of-enablement rejection, as there is no enabled scope under 35 USC § 112, first paragraph for claims 58-60, in view of the rejection, above, for lack of enablement under 35 USC § 112, first paragraph, over the issue of gene therapy.)

Claims 32-34, 36-42, 44-57, 61-64 and 66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specification, while being enabling for embodiments where the backbone of the multivalent polymer is N-2-hydroxypropylmethylacrylamide (HPMA), N-(2-hydroxyethyl)-l-glutamine (HEG) or ethyleneglycol-oligopeptide backbone, does not reasonably provide enablement for embodiments where the multivalent polymer is derived from a different polymer backbone, for reasons of record set forth in the previous Office Action, mailed 10 March 2005.

At page 12 of the amendment, Applicants argue that the specification teaches that the polymer backbone must be hydrophilic, and that the reactive groups of the backbone must complement the surface of the biological element. However, given the complexity of cells and viruses, and the uncharacterized state of the vast majority of cell surface components, and the complexity of predicting the exact folding of proteins such that the precise nature of the exposed surface of each such protein would be evident, such knowledge did not appear to be available to one of skill such as to permit practice of the claimed invention. Applicants then argue that there are a finite number of combinations. While this is logically so, there are, first of all, a presumably vast number of such combinations. Second, and more importantly, the set of embodiments encompassed may be finite, but one of skill would not be able to determine the membership of the set without undue experimentation. Applicants then cite a reference teaching dextran as the polymer. However, this is merely one embodiment, and is not commensurate in scope with the claim, and thus cannot broadly demonstrate enablement.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 60, 63 and 64 provide for the use of a polymer, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 60, 63 and 64 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 43, 47-49, 54, 64 and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 43, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 47 and 48, and therefore dependent claim 49, recite "the biologically active agent". These claims depend from claim 37, but there is no antecedent basis in claim 37 for this language. It would appear that claim 46 might have been intended as the claim from which the instant claims depend.

Claim 54 recites "an oleyl or other hydrophobic group." However, this construction renders unclear the metes and bounds of the instant claim, as it is not clear how this phrase differs from merely "a hydrophobic group". The claim might be interpreted as limited to oleyl group, or to hydrophobic groups having some unspecified similarity or homology to oleyl group, or to any hydrophobic group of any sort, all three of which interpretations being quite different in scope.

Claim 64 recites "in the agricultural industry." However, to the extent that this phrase serves to limit the scope of the claim, it is of imprecise meaning. Would methods used in agriculture only be encompassed? For example, what if a pathogen upon a non-agricultural tree were treated? The metes and bounds of the claim are very unclear as a result of this phrase.

Claim 65 sets for a Markush-type grouping, but said grouping uses the conjunction "or", which renders the metes and bounds of the claim indefinite. Substitution of "and" would overcome the rejection.

Any inquiry concerning this communication or earlier communications from the Examiner with respect to the examination on the merits should be directed to James Ketter

whose telephone number is (571) 272-0770. The Examiner normally can be reached on M-F (9:00-6:30), with alternate Fridays off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Remy Yucel, can be reached at (571) 272-0781.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jsk
January 19, 2006

JAMES KETTER
PRIMARY EXAMINER